

CLAIMS

I Claim:

1                   1.     An implantable sensor for sensing a concentration of an organic  
2 substrate, the sensor comprising:  
3                   a conductive electrode; and  
4                   a stabilized enzyme emulsion in contact with the electrode, the enzyme  
5                   emulsion comprising:  
6                   an enzyme that quantitatively oxidizes the organic substrate;  
7                   a water immiscible oxygen dissolving compound emulsified into  
8                   intimate contact with the enzyme to provide oxygen; and  
9                   a protein crosslinking agent to crosslink and insolubilize the  
10                  enzyme forming a stabilized gel comprising crosslinked  
11                  protein and particles of the oxygen dissolving substance.

1                   2.     The implantable sensor of Claim 1 further comprising a  
2 semipermeable membrane covering the electrode with the enzyme emulsion sandwiched  
3 between the membrane and the electrode.

1                   3.     The implantable sensor of Claim 1, wherein the enzyme emulsion  
2 also contains an additional carrier protein.

1                   4.     The implantable sensor of Claim 3, wherein the additional carrier  
2 protein is selected from the group consisting of serum albumin and, gelatin.

1                   5.     The implantable sensor of Claim 1, wherein the oxygen dissolving  
2 substance is selected from the group consisting of perfluorocarbons, silicone oils,  
3 fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and  
4 steroids.

1                   6.     The implantable sensor of Claim 5, wherein the oxygen dissolving  
2 substance is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl  
3 bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluoro-  
4 phenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoro-  
5 methyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluoro-  
6 trimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluoro-  
7 diisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane, perfluoro-  
8 dimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1                   7.     The implantable sensor of Claim 1, wherein the crosslinking agent  
2 is selected from the group consisting of aldehydes, carbodiimides, imidoesters,  
3 pyrocarbonates, epoxides and N-hydroxysuccinimid esters.

1                   8.     The implantable sensor of Claim 1, wherein the oxidase enzyme is  
2     selected from the group consisting of cholesterol oxidase, amino acid oxidase, alcohol  
3     oxidase, lactic acid oxidase, oxygen oxidoreductase, galactose oxidase, and glucose  
4     oxidase.

1                   9.     The implantable glucose sensor of Claim 1 further comprising an  
2     electron transport compound dissolved in the perfluorocarbon liquid.

1                   10.    The implantable glucose sensor of Claim 9, wherein the electron  
2     transport compound comprises ferrocene.

1                   11.    The implantable sensor of Claim 1, wherein the enzyme emulsion  
2     further comprises an antioxidant.

1                   12.    The implantable sensor of Claim 1, wherein the enzyme emulsion  
2     further comprises an antimicrobial agent.

1                   13.    The implantable sensor of Claim 1, wherein the enzyme emulsion  
2     further comprises an anti-inflammatory agent selected from the group consisting of  
3     steroids, lymphokines, and non-steroidal anti-inflammatory drugs.

1           14.    An implantable glucose sensor for sensing a concentration of  
2 glucose, the sensor comprising:

3           a metal electrode; and

4           a stabilized enzyme emulsion in contact with the electrode, the enzyme  
5 emulsion comprising:

6           a solution of glucose oxidase protein for oxidizing glucose to  
7           quantitatively produce hydrogen peroxide;

8           a perfluorocarbon liquid emulsified with the glucose oxidase; and

9           a crosslinking agent to crosslink covalently said protein to form a  
10 stabilized gel comprising crosslinked protein and particles of the  
11 perfluorocarbon liquid.

1           15.    The implantable glucose sensor of Claim 14 further comprising a  
2 semipermeable membrane covering the electrode with the enzyme emulsion in contact  
3 with a first surface of the membrane and sandwiched between the membrane and the  
4 electrode and with body fluids or cells in contact with a second surface of the semi-  
5 permeable membrane.

1           16.    The implantable sensor of Claim 14, wherein the oxygen  
2 dissolving substance is selected from the group consisting of perfluorocarbons, silicone  
3 oils, fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids  
4 and steroids.

1           17. The implantable sensor of Claim 16, wherein the oxygen  
2 dissolving substance is a perfluorocarbon liquid selected from the group consisting of  
3 perfluorooctyl bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane,  
4 perfluorophenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil,  
5 perfluoromethyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin,  
6 perfluorotrimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin,  
7 perfluorodiisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane,  
8 perfluorodimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1           18. The implantable glucose sensor of Claim 14 further comprising an  
2 electron transport compound dissolved in the perfluorocarbon liquid.

1           19. The implantable glucose sensor of Claim 18, wherein the electron  
2 transport compound comprises ferrocene.

1           20.    A method for producing a stabilized enzyme emulsion for use with  
2   a polarographic or amperometric sensor comprising the steps of:  
3           making an aqueous solution of a water soluble enzyme that oxidizes an  
4           organic substrate to produce hydrogen peroxide;  
5           emulsifying a volume of a water immiscible oxygen dissolving substance  
6           into the aqueous solution to form an emulsion;  
7           contacting the emulsion with a protein crosslinking agent; and  
8           spreading a mixture of the protein crosslinking agent and the emulsion  
9           into a uniform layer whereby the emulsion becomes crosslinked to  
10          form a solid gel.

1           21.    The method of Claim 20, wherein to the emulsion is contacted with  
2   a carrier protein prior to contacting with the protein crosslinking agent.

1           22.    The method of Claim 21, wherein the aqueous solution contains  
2   the carrier protein and the water soluble enzyme is added to the emulsion prior to  
3   contacting with the protein crosslinking agent.

1           23.    The method of Claim 20, wherein the oxygen dissolving substance  
2   is selected from the group consisting of perfluorocarbons, silicone oils, fluorosilicone  
3   oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and steroids.

1           24.    The method of Claim 23, wherein the 'oxygen dissolving substance  
2    is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl bromide,  
3    perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,  
4    perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,  
5    perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,  
6    perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,  
7    perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,  
8    perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1           25.    A method for producing a stabilized enzyme emulsion for use with  
2    a polarographic sensor comprising the steps of:  
3           making an aqueous solution of a carrier protein;  
4           emulsifying a volume of a perfluorocarbon liquid into the aqueous  
5           solution to form an emulsion;  
6           contacting the emulsion with a water soluble enzyme that oxidizes an  
7           organic substrate to produce hydrogen peroxide to form a mixture;  
8           contacting the mixture with a protein crosslinking agent; and  
9           spreading a mixture of the protein crosslinking agent and the emulsion  
10          into a uniform layer whereby the emulsion becomes crosslinked to  
11          form a solid gel.

- 1                   26.    The method of Claim 25, wherein the oxygen dissolving substance  
2    is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl bromide,  
3    perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,  
4    perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,  
5    perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,  
6    perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,  
7    perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,  
8    perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.